> d ibib ab 1-13

L5 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:793802 CAPLUS
DOCUMENT NUMBER: 137:305794
TITLE: **Human** and mouse ABCG8 and ABCG5 cholesterol transporters, gene sequences, mapping, mutations, coordinate regulation, and methods of use
INVENTOR(S): Hobbs, Helen H.; Shan, Bei; Barnes, Robert; Tian, Hui
PATENT ASSIGNEE(S): Tularik Inc., USA; Board of Regents, University of Texas System
SOURCE: PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002081691	A2	20021017	WO 2001-US43823	20011120

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-252235P P 20001120
US 2000-253645P P 20001128

AB The present invention provides **nucleic acids** and polypeptides for ABCG8, a novel member of the ABC family of transporter mols. ABCG8 is involved in the transport of cholesterol and other sterols, as well as other lipids, across membranes, and is assocd. with the **human** disorder **sitosterolemia**. ABCG8 sequences from **human** and mouse are provided. The genomic position of **human** (2p21) and mouse (chromosome 17) ABCG8 is also provided. Significantly, the map position of **human** ABCG8 corresponds to the map position of the **sitosterolemia**-causing gene. It is speculated that ABCG8 binds to the ABCG5 transporter to achieve sterol transport activity. ABCG5 and ABCG8 are tandemly arrayed in a head-to-head orientation, which suggest that the two genes have a bi-directional promoter. It was shown that ABCG5 and ABCG8 are regulated coordinately. There expression were found in liver and intestine in **human** and mouse. It is further speculated that, in patients with **sitosterolemia**, the gene encoding the ABCG5 moiety and/or the gene encoding the ABCG8 moiety of the ABCG5-ABCG8 heterodimer is mutated, thereby eliminating function of the heterodimer and abolishing sterol transport activity in cells. The herein-disclosed sequences can be used for any of a no. of purposes, including for the diagnosis and treatment of cholesterol-assocd. disorders, including **sitosterolemia**, and for the identification of mols. that assoc. with and/or modulate the activity of ABCG8 and ABCG5-ABCG8 heterodimer.

L5 ANSWER 2 OF 13 USPATFULL
ACCESSION NUMBER: 2002:157088 USPATFULL
TITLE: **Sitosterolemia** susceptibility gene (SSG): compositions and methods of use
INVENTOR(S): Tian, Hui, Foster City, CA, UNITED STATES
Schultz, Joshua, Half Moon Bay, CA, UNITED STATES
Shan, Bei, Redwood City, CA, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2002081687	A1	20020627	
APPLICATION INFO.:	US 2001-837992	A1	20010418	(9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-198465P	20000418 (60)
	US 2000-204234P	20000515 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: TOWNSEND AND TOWNSEND AND CREW, LLP, TWO EMBARCADERO CENTER, EIGHTH FLOOR, SAN FRANCISCO, CA, 94111-3834
NUMBER OF CLAIMS: 74
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 16 Drawing Page(s)
LINE COUNT: 3736
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides **nucleic acids** encoding a novel ABC family cholesterol transporter, SSG. The herein-disclosed sequences can be used for any of a number of purposes, including for the diagnosis and treatment of cholesterol-associated disorders, including **sitosterolemia**, and for the identification of molecules that associate with and/or modulate the activity of SSG.

L5 ANSWER 3 OF 13 CANCERLIT DUPLICATE 1
ACCESSION NUMBER: 2002155745 CANCERLIT
DOCUMENT NUMBER: 22014036 PubMed ID: 11901146
TITLE: Regulation of ATP-binding cassette sterol transporters ABCG5 and ABCG8 by the liver X receptors alpha and beta.
AUTHOR: Repa Joyce J; Berge Knut E; Pomajzl Chris; Richardson James A; Hobbs Helen; Mangelsdorf David J
CORPORATE SOURCE: Howard Hughes Medical Institute, Department of Pharmacology, University of Texas Southwestern Medical Center at Dallas, 75390, USA.
CONTRACT NUMBER: HL20948 (NHLBI)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2002 May 24) 277 (21) 18793-800.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: MEDLINE; Priority Journals
OTHER SOURCE: MEDLINE 2002295480
ENTRY MONTH: 200206
ENTRY DATE: Entered STN: 20020726
Last Updated on STN: 20021018

AB Mutations in the ATP-binding cassette (**ABC**) **transporters** ABCG5 and ABCG8 have recently been shown to cause the autosomal recessive disorder **sitosterolemia**. Here we demonstrate that the ABCG5 and ABCG8 genes are direct targets of the oxysterol receptors liver X receptor (LXR) alpha and LXRbeta. Diets containing high cholesterol markedly increased the expression of ABCG5/G8 mRNA in mouse liver and intestine. This increase was also observed using synthetic ligands of LXR and its heterodimeric partner, the retinoid X receptor. In situ hybridization analyses of tissues from LXR agonist-treated mice revealed that ABCG5/G8 mRNA is located in hepatocytes and enterocytes and is increased upon LXR activation. In addition, expression of the LXR target gene ABCA1, previously implicated in the control of cholesterol absorption, was also dramatically up-regulated in jejunal enterocytes upon exposure to LXR agonists. These changes in **ABC transporter** gene expression were not observed in mice lacking LXRs. Furthermore, in the rat hepatoma cell line FTO2B, LXR-dependent transcription of the ABCG5/G8 genes was cycloheximide-resistant, indicating that these genes are directly regulated by LXRs. The addition of ABCG5 and ABCG8 to the growing list of LXR target genes further supports the notion that LXRs serve as sterol sensors to coordinately regulate sterol catabolism, storage, efflux, and elimination.

L5 ANSWER 4 OF 13 BIOTECHNO DUPLICATE
ACCESSION NUMBER: 2002:34252331 BIOTECHNO
TITLE: Molecular cloning, genomic organization, genetic variations, and characterization of murine sterolin

genes Abcg5 and Abcg8

AUTHOR: Lu K.; Lee M.-H.; Yu H.; Zhou Y.; Sandell S.A.; Salen G.; Patel S.B.

CORPORATE SOURCE: S.B. Patel, Division of Endocrinology, Medical University of South Carolina, 114 Doughty Street, Charleston, SC 29403, United States.
E-mail: patelsb@musc.edu

SOURCE: Journal of Lipid Research, (2002), 43/4 (565-578), 39 reference(s)
CODEN: JLPRAW ISSN: 0022-2275

DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Mammalian physiological processes can distinguish between dietary cholesterol and non-cholesterol, retaining very little of the non-cholesterol in their bodies. We have recently identified two genes, ABCG5 and ABCG8, encoding sterolin-1 and -2 respectively, mutations of which cause the **human** disease **sitosterolemia**. We report here the mouse **cDNAs** and genomic organization of Abcg5 and Abcg8. Both genes are arranged in an unusual head-to-head configuration, and only 140 bases separate their two respective start-transcription sites. A single TATA motif was identified, with no canonical CCAT box present between the two genes. The genes are located on mouse chromosome 17 and this complex spans no more than 40 kb. Expression of both genes is confined to the liver and intestine. For both genes, two different sizes of transcripts were identified which differ in the lengths of their 3' UTRs. Additionally, alternatively spliced forms for Abcg8 were identified, resulting from a CAG repeat at the intron 1 splice-acceptor site, causing a deletion of a glutamine. We screened 20 different mouse strains for polymorphic variants. Although a large number of polymorphic variants were identified, strains reported to show significant differences in cholesterol absorption rates did not show significant genomic variations in Abcg5 or Abcg8.

L5 ANSWER 5 OF 13 MEDLINE
ACCESSION NUMBER: 2002162104 MEDLINE
DOCUMENT NUMBER: 21891015 PubMed ID: 11893785
TITLE: Heritability of plasma noncholesterol sterols and relationship to **DNA** sequence polymorphism in ABCG5 and ABCG8.

AUTHOR: Berge Knut E; von Bergmann Klaus; Lutjohann Dieter; Guerra Rudy; Grundy Scott M; Hobbs Helen H; Cohen Jonathan C

CORPORATE SOURCE: The Department of Molecular Genetics, UT Southwestern Medical Center, Dallas, TX 75390-9052, USA.

CONTRACT NUMBER: HL20948 (NHLBI)
HL53917 (NHLBI)

SOURCE: JOURNAL OF LIPID RESEARCH, (2002 Mar) 43 (3) 486-94.
Journal code: 0376606. ISSN: 0022-2275.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200206
ENTRY DATE: Entered STN: 20020315
Last Updated on STN: 20020823
Entered Medline: 20020625

AB The plasma concentrations of cholesterol precursor sterols and plant sterols vary over a 5- to 10-fold range among normolipidemic individuals, and provide indices of the relative rates of cholesterol synthesis and fractional absorption. In the present study, we examined the relative contributions of genetic and environmental factors to variation in the plasma concentrations and sterol-cholesterol ratios of five noncholesterol sterols, including the 5alpha-saturated derivative of cholesterol (cholestanol), two precursors in the cholesterol biosynthesis pathway (desmosterol and lathosterol), and two phytosterols (campesterol and sitosterol). Plasma sterol concentrations were highly stable in 30 individuals measured over a 48 week period. Regression of offspring sterol levels on the parental values indicated that plasma levels of all five

noncholesterol sterols were highly heritable. Analysis of monozygotic and dizygotic twin pairs also indicated strong heritability of all five sterols. Two common sequence variations (D19H and T400K) in ABCG8, an ABC half-transporter defective in **sitosterolemia**, were associated with lower concentrations of plant sterols in parents, and in their offspring.Taken together, these findings indicate that variation in the plasma concentrations of noncholesterol sterols is highly heritable, and that polymorphism in ABCG8 contributes to genetic variation in the plasma concentrations of plant sterols.

L5 ANSWER 6 OF 13 Elsevier BIOBASE COPYRIGHT 2003 Elsevier Science B.V.
ACCESSION NUMBER: 2002165984 Elsevier BIOBASE
TITLE: Comparative genome analysis of potential regulatory elements in the ABCG5-ABCG8 gene cluster
AUTHOR: Remaley A.T.; Bark S.; Walts A.D.; Freeman L.; Shulenin S.; Annilo T.; Elgin E.; Rhodes H.E.; Joyce C.; Dean M.; Santamarina-Fojo S.; Brewer Jr. H.B.
CORPORATE SOURCE: A.T. Remaley, Natl. Heart, Lung and Blood Inst., National Institutes of Health, Bldg. 10/2C-433, 10 Center Drive, Bethesda, MD 20892, United States. E-mail: aremaley@nih.gov
SOURCE: Biochemical and Biophysical Research Communications, (2002), 295/2 (276-282), 25 reference(s) CODEN: BBRCA0 ISSN: 0006-291X
PUBLISHER ITEM IDENT.: S0006291X02006526
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The excretion of sterols from the liver and intestine is regulated by the ABCG5 and ABCG8 transporters. To identify potential regulatory elements, 152 kb of the **human** ABCG5-ABCG8 gene cluster was sequenced and comparative genome analysis was performed. The two genes are oriented in a head-to-head configuration and are separated by a 374-bp intergenic region, which is highly conserved among several species. Using a reporter construct, the intergenic region was found to act as a bidirectional promoter. A conserved GATA site in the intergenic region was shown by site-directed mutagenesis to act as a repressor for the ABCG5 promoter. The intergenic region was also shown to be partially responsive to treatment by LXR agonists. In summary, several potential regulatory elements were found for the ABCG5 and ABCG8 genes, and the intergenic region was found to act as a bidirectional promoter.

L5 ANSWER 7 OF 13 SCISEARCH COPYRIGHT 2003 ISI (R)
ACCESSION NUMBER: 2001:641621 SCISEARCH
THE GENUINE ARTICLE: 460GY
TITLE: ABCA6, a novel A subclass **ABC transporter**
AUTHOR: Kaminski W E; Wenzel J J; Piehler A; Langmann T; Schmitz G (Reprint)
CORPORATE SOURCE: Univ Regensburg, Inst Clin Chem & Lab Med, Franz Josef Str Allee 11, D-93042 Regensburg, Germany (Reprint); Univ Regensburg, Inst Clin Chem & Lab Med, D-93042 Regensburg, Germany
COUNTRY OF AUTHOR: Germany
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (3 AUG 2001) Vol. 285, No. 5, pp. 1295-1301. Publisher: ACADEMIC PRESS INC, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495 USA. ISSN: 0006-291X.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 26
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Here we report the **cDNA** cloning of a novel member of the ABC A transporter subfamily from **human** macrophages. The identified coding sequence is of 5.0 kb size and contains an open reading frame which encodes a 1617 amino acid polypeptide. Structurally, the putative **ABC transporter** protein product consists of two tandemly

oriented subunits, each composed of a transmembrane domain followed by a nucleotide binding fold, and thus conforms to the group of full-size **ABC transporters**. We also demonstrate the existence of an alternative transcript that codes for a 637 amino acid protein variant bearing the features of a truncated half-size transporter. Among the **human ABC transporter** subfamily A the novel transporter shows highest protein sequence homology with ABCA8 (60%), followed by ABCA2 (32%) and ABCA1 (32%), respectively. In agreement with the proposed classification, the novel transporter was designated ABCA6. The ABCA6 gene is ubiquitously expressed with highest mRNA levels in liver, lung, heart and brain. Analysis of the genomic organization demonstrated that the ABCA6 gene is composed of 38 exons which extend across a region of 62 kb size on chromosome 17q24.2. Based on its structural features and its cholesterol-responsive regulation ABCA6 is potentially involved in macrophage lipid homeostasis. (C) 2001 Academic Press.

L5 ANSWER 8 OF 13 CANCERLIT DUPLICATE 3
ACCESSION NUMBER: 2002108426 CANCERLIT
DOCUMENT NUMBER: 21522999 PubMed ID: 11668628
TITLE: Mutations in ATP-cassette binding proteins G5 (ABCG5) and G8 (ABCG8) causing **sitosterolemia**.
AUTHOR: Hubacek J A; Berge K E; Cohen J C; Hobbs H H
CORPORATE SOURCE: Departments of Molecular Genetics and Internal Medicine and McDermott Center for Human Growth and Development, University of Texas Southwestern Medical Center at Dallas, Dallas, TX, USA.
CONTRACT NUMBER: HL20948 (NHLBI)
HL53917 (NHLBI)
SOURCE: HUMAN MUTATION, (2001 Oct) 18 (4) 359-60.
Journal code: 9215429. ISSN: 1098-1004.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: MEDLINE; Priority Journals
OTHER SOURCE: MEDLINE 2001565129
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20020726
Last Updated on STN: 20021018
AB **Sitosterolemia** is an autosomal recessive disorder caused by mutations in two adjacent genes encoding coordinately regulated ATP binding cassette (ABC) half transporters (ABCG5 and ABCG8). In this paper we describe three novel mutations causing **sitosterolemia**: 1) a frameshift mutation (c.336-337insA) in ABCG5 that results in premature termination of the protein at amino acid 197; 2) a missense mutation that changes a conserved residue c.1311C>G; N437K) in ABCG5 and 3) a splice site mutation in ABCG8 (IVS1-2A>G). This study expands the spectrum of the ABCG5 and ABCG8 mutations that cause **sitosterolemia**. Nine nonsynonymous polymorphisms are also reported: I523V, C600Y, Q604E, and M622V in ABCG5; and D19H, Y54C, T400K, A632V, and Y641F in ABCG8.

L5 ANSWER 9 OF 13 CANCERLIT DUPLICATE 4
ACCESSION NUMBER: 2002066866 CANCERLIT
DOCUMENT NUMBER: 21344600 PubMed ID: 11452359
TITLE: Two genes that map to the STSL locus cause **sitosterolemia**: genomic structure and spectrum of mutations involving sterolin-1 and sterolin-2, encoded by ABCG5 and ABCG8, respectively.
AUTHOR: Lu K; Lee M H; Hazard S; Brooks-Wilson A; Hidaka H; Kojima H; Ose L; Stalenhoef A F; Mietinnen T; Bjorkhem I; Bruckert E; Pandya A; Brewer H B Jr; Salen G; Dean M; Srivastava A; Patel S B
CORPORATE SOURCE: Division of Endocrinology, Diabetes and Medical Genetics, Medical University of South Carolina, Charleston, SC 29403, USA.
CONTRACT NUMBER: HL60616 (NHLBI)
MO1 RR01070-25 (NCRR)
SOURCE: AMERICAN JOURNAL OF HUMAN GENETICS, (2001 Aug) 69 (2)

278-90.
Journal code: 0370475. ISSN: 0002-9297.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: MEDLINE; Priority Journals
OTHER SOURCE: MEDLINE 2001400157; GENBANK-AA034046; GENBANK-AA700586; GENBANK-AF312175; GENBANK-AF312713; GENBANK-AF312714; GENBANK-AF312715; GENBANK-AF324494; GENBANK-AF324495; GENBANK-AF351785; GENBANK-AF351812; GENBANK-AF351813; GENBANK-AF351814; GENBANK-AF351815; GENBANK-AF351816; GENBANK-AF351817; GENBANK-AF351818; GENBANK-AF351819; GENBANK-AF351820; GENBANK-AF351821; GENBANK-AF351822; GENBANK-AF351823; GENBANK-AF351824; GENBANK-T99836; OMIM-210250; OMIM-605459; OMIM-605460
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20020726
Last Updated on STN: 20021018

AB **Sitosterolemia** is a rare autosomal recessive disorder characterized by (a) intestinal hyperabsorption of all sterols, including cholesterol and plant and shellfish sterols, and (b) impaired ability to excrete sterols into bile. Patients with this disease have expanded body pools of cholesterol and very elevated plasma plant-sterol species and frequently develop tendon and tuberous xanthomas, accelerated atherosclerosis, and premature coronary artery disease. In previous studies, we have mapped the STSL locus to **human** chromosome 2p21. Recently, we reported that a novel member of the **ABC-transporter** family, named "sterolin-1" and encoded by ABCG5, is mutated in 9 unrelated families with **sitosterolemia**; in the remaining 25 families, no mutations in sterolin-1 could be identified. We identified another **ABC transporter**, located <400 bp upstream of sterolin-1, in the opposite orientation. Mutational analyses revealed that this highly homologous protein, termed "sterolin-2" and encoded by ABCG8, is mutated in the remaining pedigrees. Thus, two highly homologous genes, located in a head-to-head configuration on chromosome 2p21, are involved as causes of **sitosterolemia**. These studies indicate that both sterolin-1 and sterolin-2 are indispensable for the regulation of sterol absorption and excretion. Identification of sterolin-1 and sterolin-2 as critical players in the regulation of dietary-sterol absorption and excretion identifies a new pathway of sterol transport.

L5 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 5
ACCESSION NUMBER: 2001:588364 CAPLUS
DOCUMENT NUMBER: 136:257995
TITLE: An ATP-binding cassette gene (ABCG5) from the ABCG (White) gene subfamily maps to **human** chromosome 2p21 in the region of the **sitosterolemia** locus
AUTHOR(S): Shulenin, S.; Schriml, L. M.; Remaley, A. T.; Fojo, S.; Brewer, B.; Allikmets, R.; Dean, M.
CORPORATE SOURCE: Laboratory of Genomic Diversity, NCI-Frederick, Frederick, MD, 21702, USA
SOURCE: Cytogenetics and Cell Genetics (2001), 92(3-4), 204-208
CODEN: CGCGBR; ISSN: 0301-0171
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A new **human** ATP-binding cassette (**ABC**) **transporter** gene that is highly expressed in the liver is characterized. The gene, ABCG5, contains 13 exons and encodes a 651 amino acid protein. The predicted protein is closely related to the Drosophila white gene and a **human** gene, ABCG1, which is induced by cholesterol. All members of this subfamily of genes have a single ATP-binding domain at the N-terminus and a single C-terminal set of transmembrane segments. ABCG5 maps to **human** chromosome 2p21, between the markers D2S117 and D2S119. The abundant expression of this gene in the liver suggests that the protein product has an important role

in transport of specific mol.(s) into or out of this tissue.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 11 OF 13 BIOTECHNO COPYRIGHT 2003 Elsevier Science B.V.DUPLICATE
ACCESSION NUMBER: 2001:32044523 BIOTECHNO
TITLE: Identification of a gene, ABCG5, important in the regulation of dietary cholesterol absorption
AUTHOR: Lee M.-H.; Lu K.; Hazard S.; Yu H.; Shulenin S.; Hidaka H.; Kojima H.; Allikmets R.; Sakuma N.; Pegoraro R.; Srivastava A.K.; Salen G.; Dean M.; Patel S.B.
CORPORATE SOURCE: S.B. Patel, Endocrinol. Diabet./Med. Genet. Div., Medical University of South Carolina, Charleston, SC, United States.
E-mail: patelsb@musc.edu
SOURCE: Nature Genetics, (2001), 27/1 (79-83), 22 reference(s)
CODEN: NGENEC ISSN: 1061-4036
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The molecular mechanisms regulating the amount of dietary cholesterol retained in the body, as well as the body's ability to exclude selectively other dietary sterols, are poorly understood. An average western diet will contain about 250-500 mg of dietary cholesterol and about 200-400 mg of non-cholesterol sterols. About 50-60% of the dietary cholesterol is absorbed and retained by the normal **human** body, but less than 1% of the non-cholesterol sterols are retained. Thus, there exists a subtle mechanism that allows the body to distinguish between cholesterol and non-cholesterol sterols. In **sitosterolemia**, a rare autosomal recessive disorder, affected individuals hyperabsorb not only cholesterol but also all other sterols, including plant and shellfish sterols from the intestine. The major plant sterol species is sitosterol; hence the name of the disorder. Consequently, patients with this disease have very high levels of plant sterols in the plasma and develop tendon and tuberous xanthomas, accelerated atherosclerosis, and premature coronary artery disease. We previously mapped the STSL locus to **human** chromosome 2p21 (ref. 4) and further localized it to a region of less than 2 cM bounded by markers D2S2294 and D2S2291 (M.-H.L et al., manuscript submitted). We now report that a new member of the **ABC transporter** family, ABCG5, is mutant in nine unrelated **sitosterolemia** patients.

L5 ANSWER 12 OF 13 PROMT COPYRIGHT 2003 Gale Group

ACCESSION NUMBER: 2000:1044594 PROMT
TITLE: RARE LIPID DISORDER HINTS AT CHOLESTEROL-CUTTING AGENTS TULARIK, TEXAS U. TEAM UP TO FERRET OUT GENES THAT HUSTLE TOXIC PLANT STEROLS OUT OF BODY.
AUTHOR(S): Leff, David N.
SOURCE: BIOWORLD Today, (1 Dec 2000) No. 231.
PUBLISHER: American Health Consultants, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 1039
FULL TEXT IS AVAILABLE IN THE ALL FORMAT
AB Q: What do the following foods have in common: Nuts, seeds, chocolate, olives, avocado, corn oil, wheat germ, yams?
THIS IS THE FULL TEXT: COPYRIGHT 2000 American Health Consultants, Inc.

Subscription: $1350.00 per year. Published daily (5 times a week).

L5 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 7
ACCESSION NUMBER: 2000:887286 CAPLUS
DOCUMENT NUMBER: 134:145866
TITLE: Accumulation of dietary cholesterol in **sitosterolemia** caused by mutations in adjacent **ABC transporters**

AUTHOR(S): Berge, Knut E.; Tian, Hui; Graf, Gregory A.; Yu, Liqing; Grishin, Nick V.; Schultz, Joshua; Kwiterovich, Peter; Shan, Bei; Barnes, Robert; Hobbs, Helen H.
CORPORATE SOURCE: Dep. Molecular Genetics and McDermott Center for Human Growth, Univ. Texas Southwestern Med. Center Dallas, Dallas, TX, 75390-9046, USA
SOURCE: Science (Washington, D. C.) (2000), 290(5497), 1771-1775
CODEN: SCIEAS; ISSN: 0036-8075
PUBLISHER: American Association for the Advancement of Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In healthy individuals, acute changes in cholesterol intake produce modest changes in plasma cholesterol levels. A striking exception occurs in **sitosterolemia**, an autosomal recessive disorder characterized by increased intestinal absorption and decreased biliary excretion of dietary sterols, hypercholesterolemia, and premature coronary atherosclerosis. The authors identified seven different mutations in two adjacent, oppositely oriented genes that encode new members of the ATP-binding cassette (**ABC**) **transporter** family (six mutations in ABCG8 and one in ABCG5) in nine patients with **sitosterolemia**. The two genes are expressed at highest levels in liver and intestine and, in mice, cholesterol feeding up-regulates expressions of both genes. These data suggest that ABCG5 and ABCG8 normally cooperate to limit intestinal absorption and to promote biliary excretion of sterols, and that mutated forms of these transporters predispose to sterol accumulation and atherosclerosis.
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib ab 1-7

L6 ANSWER 1 OF 7 BIOTECHNO COPYRIGHT 2003 Elsevier Science B.V.
ACCESSION NUMBER: 2001:32044523 BIOTECHNO
TITLE: Identification of a gene, ABCG5, important in the regulation of dietary cholesterol absorption
AUTHOR: Lee M.-H.; Lu K.; Hazard S.; Yu H.; Shulenin S.; Hidaka H.; Kojima H.; Allikmets R.; Sakuma N.; Pegoraro R.; Srivastava A.K.; Salen G.; Dean M.; Patel S.B.
CORPORATE SOURCE: S.B. Patel, Endocrinol. Diabet./Med. Genet. Div., Medical University of South Carolina, Charleston, SC, United States.
E-mail: patelsb@musc.edu
SOURCE: Nature Genetics, **(2001)**, 27/1 (79-83), 22 reference(s)
CODEN: NGENEC ISSN: 1061-4036
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The molecular mechanisms regulating the amount of dietary cholesterol retained in the body, as well as the body's ability to exclude selectively other dietary sterols, are poorly understood. An average western diet will contain about 250-500 mg of dietary cholesterol and about 200-400 mg of non-cholesterol sterols. About 50-60% of the dietary cholesterol is absorbed and retained by the normal **human** body, but less than 1% of the non-cholesterol sterols are retained. Thus, there exists a subtle mechanism that allows the body to distinguish between cholesterol and non-cholesterol sterols. In **sitosterolemia**, a rare autosomal recessive disorder, affected individuals hyperabsorb not only cholesterol but also all other sterols, including plant and shellfish sterols from the intestine. The major plant sterol species is sitosterol; hence the name of the disorder. Consequently, patients with this disease have very high levels of plant sterols in the plasma and develop tendon and tuberous xanthomas, accelerated atherosclerosis, and premature coronary artery disease. We previously mapped the STSL locus to **human** chromosome 2p21 (ref. 4) and further localized it to a region of less than 2 cM bounded by markers D2S2294 and D2S2291 (M.-H.L et al., manuscript submitted). We now report that a new member of the **ABC transporter** family, ABCG5, is mutant in nine unrelated **sitosterolemia** patients.

L6 ANSWER 2 OF 7 CANCERLIT
ACCESSION NUMBER: 2002108426 CANCERLIT
DOCUMENT NUMBER: 21522999 PubMed ID: 11668628
TITLE: Mutations in ATP-cassette binding proteins G5 (ABCG5) and G8 (ABCG8) causing **sitosterolemia**.
AUTHOR: Hubacek J A; Berge K E; Cohen J C; Hobbs H H
CORPORATE SOURCE: Departments of Molecular Genetics and Internal Medicine and McDermott Center for Human Growth and Development, University of Texas Southwestern Medical Center at Dallas, Dallas, TX, USA.
CONTRACT NUMBER: HL20948 (NHLBI)
HL53917 (NHLBI)
SOURCE: HUMAN MUTATION, **(2001 Oct)** 18 (4) 359-60.
Journal code: 9215429. ISSN: 1098-1004.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: MEDLINE; Priority Journals
OTHER SOURCE: MEDLINE 2001565129
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20020726
Last Updated on STN: 20021018
AB **Sitosterolemia** is an autosomal recessive disorder caused by mutations in two adjacent genes encoding coordinately regulated ATP binding cassette (ABC) half transporters (ABCG5 and ABCG8). In this paper we describe three novel mutations causing **sitosterolemia**: 1) a

frameshift mutation (c.336-337insA) in ABCG5 that results in premature termination of the protein at amino acid 197; 2) a missense mutation that changes a conserved residue c.1311C>G; N437K) in ABCG5 and 3) a splice site mutation in ABCG8 (IVS1-2A>G). This study expands the spectrum of the ABCG5 and ABCG8 mutations that cause **sitosterolemia**. Nine nonsynonymous polymorphisms are also reported: I523V, C600Y, Q604E, and M622V in ABCG5; and D19H, Y54C, T400K, A632V, and Y641F in ABCG8.

L6 ANSWER 3 OF 7 CANCERLIT
ACCESSION NUMBER: 2002066866 CANCERLIT
DOCUMENT NUMBER: 21344600 PubMed ID: 11452359
TITLE: Two genes that map to the STSL locus cause **sitosterolemia**: genomic structure and spectrum of mutations involving sterolin-1 and sterolin-2, encoded by ABCG5 and ABCG8, respectively.
AUTHOR: Lu K; Lee M H; Hazard S; Brooks-Wilson A; Hidaka H; Kojima H; Ose L; Stalenhoef A F; Mietinnen T; Bjorkhem I; Bruckert E; Pandya A; Brewer H B Jr; Salen G; Dean M; Srivastava A; Patel S B
CORPORATE SOURCE: Division of Endocrinology, Diabetes and Medical Genetics, Medical University of South Carolina, Charleston, SC 29403, USA.
CONTRACT NUMBER: HL60616 (NHLBI)
MO1 RR01070-25 (NCRR)
SOURCE: AMERICAN JOURNAL OF HUMAN GENETICS, **(2001 Aug)** 69 (2) 278-90.
Journal code: 0370475. ISSN: 0002-9297.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: MEDLINE; Priority Journals
OTHER SOURCE: MEDLINE 2001400157; GENBANK-AA034046; GENBANK-AA700586; GENBANK-AF312175; GENBANK-AF312713; GENBANK-AF312714; GENBANK-AF312715; GENBANK-AF324494; GENBANK-AF324495; GENBANK-AF351785; GENBANK-AF351812; GENBANK-AF351813; GENBANK-AF351814; GENBANK-AF351815; GENBANK-AF351816; GENBANK-AF351817; GENBANK-AF351818; GENBANK-AF351819; GENBANK-AF351820; GENBANK-AF351821; GENBANK-AF351822; GENBANK-AF351823; GENBANK-AF351824; GENBANK-T99836; OMIM-210250; OMIM-605459; OMIM-605460
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20020726
Last Updated on STN: 20021018

AB **Sitosterolemia** is a rare autosomal recessive disorder characterized by (a) intestinal hyperabsorption of all sterols, including cholesterol and plant and shellfish sterols, and (b) impaired ability to excrete sterols into bile. Patients with this disease have expanded body pools of cholesterol and very elevated plasma plant-sterol species and frequently develop tendon and tuberous xanthomas, accelerated atherosclerosis, and premature coronary artery disease. In previous studies, we have mapped the STSL locus to **human** chromosome 2p21. Recently, we reported that a novel member of the **ABC-transporter** family, named "sterolin-1" and encoded by ABCG5, is mutated in 9 unrelated families with **sitosterolemia**; in the remaining 25 families, no mutations in sterolin-1 could be identified. We identified another **ABC transporter**, located <400 bp upstream of sterolin-1, in the opposite orientation. Mutational analyses revealed that this highly homologous protein, termed "sterolin-2" and encoded by ABCG8, is mutated in the remaining pedigrees. Thus, two highly homologous genes, located in a head-to-head configuration on chromosome 2p21, are involved as causes of **sitosterolemia**. These studies indicate that both sterolin-1 and sterolin-2 are indispensable for the regulation of sterol absorption and excretion. Identification of sterolin-1 and sterolin-2 as critical players in the regulation of dietary-sterol absorption and excretion identifies a new pathway of sterol transport.

L6 ANSWER 4 OF 7 CAPLUS

ACCESSION NUMBER: 2001:588364 CAPLUS
DOCUMENT NUMBER: 136:257995
TITLE: An ATP-binding cassette gene (ABCG5) from the ABCG (White) gene subfamily maps to **human** chromosome 2p21 in the region of the **sitosterolemia** locus
AUTHOR(S): Shulenin, S.; Schriml, L. M.; Remaley, A. T.; Fojo, S.; Brewer, B.; Allikmets, R.; Dean, M.
CORPORATE SOURCE: Laboratory of Genomic Diversity, NCI-Frederick, Frederick, MD, 21702, USA
SOURCE: Cytogenetics and Cell Genetics (**2001**), 92(3-4), 204-208
CODEN: CGCGBR; ISSN: 0301-0171
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A new **human** ATP-binding cassette (**ABC**) **transporter** gene that is highly expressed in the liver is characterized. The gene, ABCG5, contains 13 exons and encodes a 651 amino acid protein. The predicted protein is closely related to the Drosophila white gene and a **human** gene, ABCG1, which is induced by cholesterol. All members of this subfamily of genes have a single ATP-binding domain at the N-terminus and a single C-terminal set of transmembrane segments. ABCG5 maps to **human** chromosome 2p21, between the markers D2S117 and D2S119. The abundant expression of this gene in the liver suggests that the protein product has an important role in transport of specific mol.(s) into or out of this tissue.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:887286 CAPLUS
DOCUMENT NUMBER: 134:145866
TITLE: Accumulation of dietary cholesterol in **sitosterolemia** caused by mutations in adjacent **ABC transporters**
AUTHOR(S): Berge, Knut E.; Tian, Hui; Graf, Gregory A.; Yu, Liqing; Grishin, Nick V.; Schultz, Joshua; Kwiterovich, Peter; Shan, Bei; Barnes, Robert; Hobbs, Helen H.
CORPORATE SOURCE: Dep. Molecular Genetics and McDermott Center for Human Growth, Univ. Texas Southwestern Med. Center Dallas, Dallas, TX, 75390-9046, USA
SOURCE: Science (Washington, D. C.) (**2000**), 290(5497), 1771-1775
CODEN: SCIEAS; ISSN: 0036-8075
PUBLISHER: American Association for the Advancement of Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In healthy individuals, acute changes in cholesterol intake produce modest changes in plasma cholesterol levels. A striking exception occurs in **sitosterolemia**, an autosomal recessive disorder characterized by increased intestinal absorption and decreased biliary excretion of dietary sterols, hypercholesterolemia, and premature coronary atherosclerosis. The authors identified seven different mutations in two adjacent, oppositely oriented genes that encode new members of the ATP-binding cassette (**ABC**) **transporter** family (six mutations in ABCG8 and one in ABCG5) in nine patients with **sitosterolemia**. The two genes are expressed at highest levels in liver and intestine and, in mice, cholesterol feeding up-regulates expressions of both genes. These data suggest that ABCG5 and ABCG8 normally cooperate to limit intestinal absorption and to promote biliary excretion of sterols, and that mutated forms of these transporters predispose to sterol accumulation and atherosclerosis.
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 7 PROMT COPYRIGHT 2003 Gale Group

ACCESSION NUMBER: 2000:1044594 PROMT
TITLE: RARE LIPID DISORDER HINTS AT CHOLESTEROL-CUTTING AGENTS TULARIK, TEXAS U. TEAM UP TO FERRET OUT GENES THAT HUSTLE TOXIC PLANT STEROLS OUT OF BODY.
AUTHOR(S): Leff, David N.
SOURCE: BIOWORLD Today, (**1 Dec 2000**) No. 231.
PUBLISHER: American Health Consultants, Inc.
DOCUMENT TYPE: Newsletter
LANGUAGE: English
WORD COUNT: 1039
FULL TEXT IS AVAILABLE IN THE ALL FORMAT

AB Q: What do the following foods have in common: Nuts, seeds, chocolate, olives, avocado, corn oil, wheat germ, yams?

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L6 ANSWER 7 OF 7 SCISEARCH COPYRIGHT 2003 ISI (R)
ACCESSION NUMBER: 2001:641621 SCISEARCH
THE GENUINE ARTICLE: 460GY
TITLE: ABCA6, a novel A subclass **ABC transporter**
AUTHOR: Kaminski W E; Wenzel J J; Piehler A; Langmann T; Schmitz G (Reprint)
CORPORATE SOURCE: Univ Regensburg, Inst Clin Chem & Lab Med, Franz Josef Str Allee 11, D-93042 Regensburg, Germany (Reprint); Univ Regensburg, Inst Clin Chem & Lab Med, D-93042 Regensburg, Germany
COUNTRY OF AUTHOR: Germany
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (**3 AUG 2001**) Vol. 285, No. 5, pp. 1295-1301.
Publisher: ACADEMIC PRESS INC, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495 USA.
ISSN: 0006-291X.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 26
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Here we report the **cDNA** cloning of a novel member of the ABC A transporter subfamily from **human** macrophages. The identified coding sequence is of 5.0 kb size and contains an open reading frame which encodes a 1617 amino acid polypeptide. Structurally, the putative **ABC transporter** protein product consists of two tandemly oriented subunits, each composed of a transmembrane domain followed by a nucleotide binding fold, and thus conforms to the group of full-size **ABC transporters**. We also demonstrate the existence of an alternative transcript that codes for a 637 amino acid protein variant bearing the features of a truncated half-size transporter. Among the **human ABC transporter** subfamily A the novel transporter shows highest protein sequence homology with ABCA8 (60%), followed by ABCA2 (32%) and ABCA1 (32%), respectively. In agreement with the proposed classification, the novel transporter was designated ABCA6. The ABCA6 gene is ubiquitously expressed with highest mRNA levels in liver, lung, heart and brain. Analysis of the genomic organization demonstrated that the ABCA6 gene is composed of 38 exons which extend across a region of 62 kb size on chromosome 17q24.2. Based on its structural features and its cholesterol-responsive regulation ABCA6 is potentially involved in macrophage lipid homeostasis. (C) 2001 Academic Press.